THE DEPARTMENT OF THE HOSPITAL

Dr. Rivers, Director

STUDIES ON PNEUMOCOCCI

Dr. Avery and associates.

To demonstrate the transformation of one pneumococcal type to another, the following minimal requirements must be supplied: Pneumococci of a competent R strain inoculated into a medium adequate for growth containing anti-R agglutinins, a factor found in serous fluids, and a specific transforming principle. The transforming principle is obtained from a smooth culture of a specific type of pneumococcus. Thus, if one wishes to transform a Type II pneumococcus to a Type III pneumococcus, the specific transforming substance used in the experiment must come from a smooth culture of Type III organisms. Dr. Avery and his associates devoted most of their time during the past year to a search for further evidence that the transforming principle is in reality a highly polymerized desoxyribonucleic acid.

Chemical analysis was made of an initial concentrate, approximately 300 milligrams, obtained from 225 liters of Type III pneumococcus culture. The purified material finally recovered showed activity at 0.01 milligram per cc., and 0.07 milligram per cc. was approximately the amount which consistently gave transformation in 50 per cent of the tests in a system optimum in other respects. It is of special interest that, during the treatments which this active material had received, its amino acid content steadily fell until less than 0.5 per cent of the nitrogen present was amino acid nitrogen. Although a protein material of exceedingly high activity might still have been present, it appears quite unlikely that nonspecific fractionation procedures which were successfully removing

protein material in general should simultaneously have been causing enrichment of a hypothetical active protein. All tests point to the fact that most of the material with which the work was done consisted of desoxyribonucleic acid.

Present conceptions of the nature of nucleic acids are of two divergent kinds. On the one hand, it has long been stated that all, irrespective of source, are polymers of one of two simple structures. Either they are composed of units containing one residue each of adenine, guanine, cytosine, and uracil, combined with four ribose and phosphate residues; or they have the desoxyribonucleic structure made up of one residue each of adenine, guanine, cytosine, and thiamine, with four desoxyribose and phosphate groups. Contrasting with this view is the opinion that, for example, desoxyribonucleic acids from biologically different sources possess structures characteristic of their sources, differing quantitatively and perhaps even qualitatively from the composition of the classical structure. This latter view derives its support from a few observations of ratios of purine bases deviating materially from the theoretical and in one or two reports of a discovery of unusual bases in nucleic acid preparations. Also, the conception that the pneumococcus-transforming principle is a desoxyribonucleic acid implies the corollary that even each such preparation from a distinct serological type of pneumococcus must have a unique chemical or physical structure. Using a paper chromatographic technic devised by them for the study of nucleic acids, Dr. Avery and his associates have found evidence that the desoxyribonucleic acids from specific types of pneumococci vary from the classical structure. If these findings are confirmed by further work, a step forward will have been made in understanding the biological specificity of nucleic acids.

In last year's report the active factor in serous fluids was stated to be albumin. It has long been known that all serous fluids are not active in transforming experiments, although albumin is always present in such fluids. There may be a number of reasons why different serous fluids act so differently in experiments of this nature. Some of the reasons have been discovered. For instance, small amounts of lauric or oleic acids can inhibit transformation in a system containing fifty times their weight of albumin. Also globulin fractions in the fluids may inhibit the reaction. Furthermore, it has been shown that excessive amounts of albumin itself will interfere with transformation. This last fact is very interesting because a certain amount of albumin is necessary for transformation. The interference in this instance has been shown to be due to a slow inactivation of the transforming principle when incubated in the presence of albumin. It is not known how the inactivation is brought about. In any event, these observations are compatible with the conception that some reaction between albumin and nucleic acid is important for the success of transformation, but that in its latter stages the reaction leads to inactivation of the transforming principle.

In a previous report it was stated that washed pneumococci, when supplied with glucose and amino acids, do not multiply but synthesize and accumulate cell protein. The energy furnished by the oxidation of glucose is an essential factor making possible this synthesis. An attempt has been made to learn whether the breakdown of glucose can also facilitate the coupling of purine and pyrimidine bases to sugar and phosphate with formation of nucleic acid. Experiments of this kind have been successful; but a lack of nucleic acid in the bacterial cells must be developed first. This can be done in at least one of two ways. Studies of this kind may reveal

something of the integration of chemical processes in normal growth in general and of a sequence of events that are very likely occurring during pneumococcal transformation in particular.

RESPIRATORY DISEASES

Dr. Horsfall and associates.

Two types of virus have been shown to cause influenza, namely, influenza A virus and influenza B virus. Vaccines against these two viruses have been shown to protect lower animals, and there is evidence that these vaccines under certain conditions will protect man against epidemics of influenza. However, in 1947, influenza A virus was active in many localities in the United States and, much to the surprise of many workers, persons who had been vaccinated against influenza A virus developed the disease as frequently as did those who had not been vaccinated. Strains of virus isolated from these outbreaks proved to be influenza A virus differing markedly from the usual type of influenza A virus, and could be identified as such only by the use of convalescent human serum. Furthermore, it was shown that the standard vaccine against influenza A would not protect against the influenza A strain isolated during 1947.

In January, 1948, one month after an extensive epidemic in Los Angeles but before strains from it had been received in New York, a small outbreak of acute respiratory infection (10 cases) developed among employees of the Rockefeller Institute. Seven of these patients were studied in the Rockefeller Hospital; 2 of them had primary atypical pneumonia; the others had influenza and from two of them strains of influenza A virus were recovered. Neither of the two 1948 strains of virus could be identified *in vitro* by use of specific immune serum against pre-1947 strains. One 1948 strain gave specific reactions *in vitro* with